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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,693	09/14/2000	Sathasivan Indiran Pather	CIMA 3.0-030 CONT II	2096

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CIMA
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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/661,693	PATHER ET AL.	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,25-27,30-33,83,86,88,91,93,94 and 105* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22, 25-27, 30-33, 83, 86, 88, 91, 93, 94, 105* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments and remarks received in the office on 5/30/2007 amending claims 22, 33 and 86, adding claim 105, and canceling claim 84. Claims 22, 25-27, 30-33, 83, 86, 88, 91, 93, 94, 105 are pending.

Applicants' arguments' regarding the rejection of claims 22, 26, 27, 30-33, 83, 84, 86, 88, 91, 93, and 94 under 35 U.S.C. 103(a) as being unpatentable over McCarty in view of Wehling et al. and further in view of Streisand et al. have been fully considered but they are not persuasive. The rejection is maintained for the reasons of the record. Applicants' arguments' regarding the rejection of claims 22, 25-27, 30-33, 83, 84, 86, 88, 91, 93, and 94 under 35 U.S.C. 103(a) as being unpatentable over Chen et al. in view of Wehling et al. and further in view of Streisand et al. have been fully considered but they are not persuasive. The rejection is maintained for the reasons of the record. Applicants' arguments' regarding the rejection of claims 22, 30, 84, 86, 91, 93 and 94 under 35 U.S.C. 103(a) as being unpatentable over McCarty in view of Streisand et al. and further in view of Gazzaniga et al. have been found to be persuasive and the rejection is withdrawn. The double patenting rejections are maintained as the applicants have not filed a Terminal Disclaimer. The limitations of the amended claims and additional new claim 105 fall within the scope of the rejected claims hence have been rejected under the same 35 U.S.C 103 rejections that were made in the previous office action (non-final rejection). In view of applicants' amendments and addition of new claims a modified 35 U.S.C 103(a) rejection is now made. The office action is made final.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22, 25-27, 30-33, 83, 84, 86, 88, 91, 93, 94 and 105 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 11/026,327 ('327). Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed invention overlaps with that previously claimed. Specifically, claims 1-22 of '327 are directed to a method of making the product claimed in the instant claims. The product claims of the instant invention are obvious over the claims directed to a method of making such product because the method claims of '327 recite the product claimed herein.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 22, 25-27, 30-33, 83, 84, 86, 88, 91, 93, 94 and 105 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 11/026,132 ('132)

The instant application teaches a tablet comprising fentanyl, at least one pH adjusting substance and saliva activated effervescent couple and the co-pending application '132 teaches a tablet comprising fentanyl, effervescent couple and pH adjusting substance.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed invention overlaps with that previously claimed. Thus, the copending application is directed to fentanyl, an effervescent dosage form, which anticipate the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 22, 25-27, 30-33, 83, 84, 86, 88, 91, 93, 94 and 105 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 11/027,353 ('353).

The instant application teaches a tablet comprising fentanyl, at least one pH adjusting substance and saliva activated effervescent couple and the co-pending application '353 teaches a dosage form comprising fentanyl, an effervescent couple and pH adjusting substance.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed invention overlaps with that previously claimed. Thus, the copending application is directed to fentanyl, an effervescent dosage form, which anticipate the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 22, 25-27, 30-33, 83, 84, 86, 88, 91, 93, 94 and 105 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27, 29-33 of copending Application No. 11, 511, 098 ('098).

The instant application teaches a tablet comprising fentanyl, at least one pH adjusting substance and saliva activated effervescent couple and the co-pending application '098 teaches a tablet comprising fentanyl, an effervescent couple and pH adjusting substance.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed invention overlaps with that of the co-pending application. The copending application is directed to fentanyl tablet, an effervescent dosage form, which anticipate the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22, 26, 27, 30-33, 83, 84, 86, 88, 91, 93, 94 and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCarty (US 5,073,374) in view of Wehling et al. (WO 91104757) and further in view of Streisand et al. (Buccal absorption of fentanyl is pH-dependent in dogs', Anesthesiology, (1995 Mar), 82 (3), pp. 759-64).

McCarty teaches fast dissolving buccal tablets particularly useful for the administration of active ingredients that show poor bioavailability upon administration through non-parenteral modes (See Abstract). Such active ingredients include analgesics such as fentanyl (col. 1, lines 14-30). The tablets of McCarty are placed in the buccal pouch of the oral cavity and allowed to dissolve (col. 4, lines 3-7).

McCarty does not teach the effervescent couple of the instant claims.

Wehling et al. teach effervescent dosage forms for direct oral administration (i.e. for direct insertion into the mouth of a patient), which comprise at least one systemically distributable ingredient (e.g. a drug), effervescent disintegration agents (a soluble acid source and a carbonate source) and adjuvants such as binders, flavors, colors, fillers, non-effervescent disintegrants, etc. (p. 3, lines 30-37; p. 11, lines 22-38; p. 12, lines 1-19; p. 14, lines 25-37; p. 15). The reference further teaches that in preferred embodiments the effervescent disintegration agent may include, without limitation, at least one acid selected from the group consisting of citric acid, tartaric acid, malic acid, fumaric acid, adipic acid, succinic acid, acid anhydrides and acid salts and mixtures thereof, and at least one base selected from the group consisting of carbonate salts, bicarbonate salts and mixtures thereof (p 6, lines 7-14, p 12, lines 2-19). The reference teaches that carbonate sources include sodium bicarbonate, sodium carbonate,

potassium carbonate, magnesium carbonate etc (p 12, lines 13-19). Analgesics are among the drugs that can be administered in oral effervescent dosage forms of Wehling et al. (p. 9, line 29). The amount of the effervescent disintegration agents is 5-50% by weight, and the amount of either acid or carbonate source may exceed the amount of the other component (p. 12, lines 20-36; p. 13, lines 3-12). "This may be useful to enhance taste and/or performance of a tablet containing an overage of either component" (p. 12, lines 36-38). The tablets of Wehling et al. dissolve in the mouth in between about 30 seconds and about 7 minutes (p. 13, lines 13-24). Wehling et al. teach that the use of the effervescent disintegration agents provides the following benefits: masking the objectionable flavor of medicaments, facilitating the disintegration of the tablet and providing pleasant organoleptic sensation (p. 6, lines 15-26). Further, such dosage forms are particularly useful in administration of medications to patients who cannot or will not chew, such as children and the elderly (p. 4, lines 9-25).

Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to modify the fast dissolving buccal fentanyl tablets of McCarty such that to employ effervescent disintegration agents. One having ordinary skill in the art would have been motivated to do this to obtain even faster dissolution as well as masking the objectionable flavor of medicaments and providing pleasant organoleptic sensation as suggested by Wehling et al. Further, while suggesting that the amount of either acid or carbonate source may exceed the amount of the other component in order to enhance taste and/or performance of a tablet

containing an overage of either component, the Wehling reference does not explicitly teach the at least one pH adjusting substance which is a base as claimed herein.

Streisand et al. teach that the buccal absorption, bioavailability and permeability of fentanyl are pH dependent and increase as the pH of the fentanyl solution becomes more basic, which is due to an increase in the fraction of unionized fentanyl (Abstract; Discussion). The reference further teaches that fentanyl citrate is a weak base, it may be possible to speed absorption by increasing the pH of the delivery vehicle, thus converting more fentanyl to the unionized form and in theory unionized drugs pass through biologic membranes more easily than ionized drugs (p 760, lines 2-9). The reference teaches the administration of fentanyl citrate to dogs through the buccal mucosa (p 760, col.2, lines 9-10).

Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to modify the teachings of Wehling et al. such as to employ the excess of the carbonate source (base). One having ordinary skill in the art would have been motivated to do this to obtain basic pH as which the buccal absorption, bioavailability and permeability of fentanyl increase, thus making the tablet more effective, as suggested by Streisand et al. With respect to Claims 93 and 94, which recite tablet "adapted for" gingival and sublingual administration, respectively, these types of administration are obvious variations of oral transmucosal administration. Therefore, Claims 93 and 94 don't recite any additional ingredients and/or characteristics, therefore, the combination of references discussed above meets the claimed limitations.

Claims 22, 25-27, 30-33, 83, 84, 86, 88, 91, 93, 94 and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. ('Studies on formulations of fentanyl buccal adhesive tablets", Zhongguo Yiyao Gongye Zazhi, 1997, 28(3), 129-1311) in view of Wehling et al. (WO 91104757) and further in view of Streisand et al. ("Buccal absorption of fentanyl is pH-dependent in dogs', Anesthesiology, (1995 Mar), 82 (3), pp. 759-64).

Chen et al. teach fentanyl citrate buccal adhesive tablets (see Abstract). Chen et al. do not teach the effervescent couple of the instant claims.

Wehling et al. teach effervescent dosage forms for direct oral administration as discussed above.

Streisand et al. teach that the buccal absorption, bioavailability and permeability of fentanyl are pH dependent and increase as the pH of the fentanyl solution becomes more basic as discussed above.

Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to modify the adhesive buccal fentanyl tablets of Chen et al. such that to employ effervescent disintegration agents. One having ordinary skill in the art would have been motivated to do this to obtain even faster dissolution as well as masking the objectionable flavor of medicaments and providing pleasant organoleptic sensation as suggested by Wehling et al. Further, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to modify the teachings of Wehling et al. such as to employ the excess of the carbonate source (base). One having ordinary skill in the art would have

been motivated to do this to obtain basic pH as which the buccal absorption, bioavailability and permeability of fentanyl increase, thus making the tablet more effective, as suggested by Streisand et al. With respect to Claims 93 and 94, which recite tablet "adapted for" gingival and sublingual administration, respectively, these types of administration are obvious variations of oral transmucosal administration. Therefore, Claims 93 and 94 don't recite any additional ingredients and/or characteristics, therefore, the combination of references discussed above meets the claimed limitations.

Response to Arguments

Applicant's arguments with respect to 103 rejections have been considered but are not persuasive. Applicants' argue that McCarty is silent on the use of effervescent couples and does not teach or suggest pH adjustment as part of its delivery technology. In response, McCarty's deficiencies are overcome by the combined teachings of McCarty, Wehling and Streisand. Wehling et al. teaches the use of the effervescent agents in analgesic formulations to provide disintegration of the tablet and teaches the acids and bases of the effervescent couple claimed in the instant application and Streisand clearly teaches that buccal absorption of fentanyl is pH dependent and the absorption, bioavailability and permeability of fentanyl are markedly increased as the pH of the fentanyl solution becomes more basic, which is due to an increase in the fraction of unionized fentanyl. Also the prior art of record clearly teaches that the use of the effervescent disintegration agents in analgesic formulations provides the following benefits: masking the objectionable flavor of medicaments, facilitating the disintegration

of the tablet and providing pleasant organoleptic sensation. See Wehling et al. One of ordinary skill in the art at the time of the invention would be motivated to increase the buccal absorption, bioavailability and permeability of fentanyl by increasing the pH by routine experimentation. It would have been obvious to one of ordinary skill in the art to combine teachings of McCarty, Wehling and Streisand to make a composition comprising fentanyl, pH adjusting agent and effervescent couple as the prior art clearly teaches the buccal administration of fentanyl and Streisand teaches that adjusting pH increases absorption, bioavailability and permeability of fentanyl and Wehling teaches the disintegration of effervescent tablets.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin,* 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

No claims are allowed.

Applicants' amendment and addition of a new claim necessitated the modified rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL.

See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER
8/13/07